DEPARTMENT OF INTERNAL MEDICINE,

COLLEGE OF MEDICINE AND HEALTH SCIENCES

UNIVERSITY OF GONDAR

VISCERAL LEISHMANIASIS-HUMAN IMMUNO DEFICIENCY VIRUS COINFECTION AND ASSOCIATED FACTORS AMONG VISCERAL LEISHMANIASIS PATIENTS AT UNIVERSITY OF GONDAR HOSPITAL

BY: GIRMA WOREDE

ADVISORS:

1. **Dr. ERMIAS DIRO**
2. **Ato TERESA KISI**

A THESIS SUBMITTED TO DEPARTMENT OF INTERNAL MEDICINE, COLLEGE OF MEDICINE AND HEALTH SCIENCES, UNIVERSITY OF GONDAR IN PARTIAL FULLFILLMENT OF THE REQUIREMENTS FOR MASTERS IN CLINICAL TROPICAL INFECTIOUS DISEASES AND HIV MEDICINE.

August, 2014

GONDAR, ETHIOPIA

UNIVERSITY OF GONDAR

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DEPARTMENT OF INTERNAL MEDICINE

ASSESSMENT OF VISCERAL LEISHMANIASIS-HIV COINFECTION AND ASSOCIATED FACTORS OF VISCERAL LEISHMANIASIS PATEINTS AT UNIVERSITY OF GONDAR HOSPITAL

By:- Girma Worede _____

Address:- Tel. 0918035871

E- Mail:- girmaworede@yahoo.com

Advisors:

1. Dr. ERMIAS DIRO_____

2. Ato TERESA KISI _____

Name of Examiner **signature**

_____ _____

Acknowledgement

I would like to express my gratitude for department of internal medicine for helping me in the selection of my research topic and assigning of advisors.

In addition I am grateful to my advisors Dr. Ermias Diro and Ato Teresa Kisi for their unreserved assistance in commenting the thesis paper.

Furthermore I pass my sincere thanks to Ato Yegnasew Takele, who is a member staff of University of Gondar, Leishmaniasis Research and Treatment Center (LRTC) for his involvement in correcting my draft proposal. I also thank all staff members of the LRTC for encouraging me to keep up on my proposal. I would like thank Ato Ashenafi Takele for helping and suggesting me in the process of writing the research proposal.

Finally I would like to extend my appreciation to my families and friends for their encouragement throughout the study period to reach this final stage.

Table of content

ACRONYMS:

AIDS:	Acquired Immune Deficiency Syndrome
BMI:	Body Mass Index
HIV:	Human immune deficiency virus
LD:	Leis mania *Donovani*
L. *infantum*:	Leis mania *infantum*
LRTC:	Leishmaniasis Research and Treatment Center
MSF:	Médecins Sans Frontières
SNNPR:	Southern Nation's Nationalities People Republic
SGPT:	Serum Glutamic Pyruvic Transaminase
SGOT:	Serum Glutamic-Oxalacetic Transaminase
TLS:	Total Liver Span
UoGH:	University of Gondar Hospital
VL:	Visceral Leishmaniasis
WBC:	White Blood Cell
WHO:	World Health Organization
HAPCO:	HIV/AIDS prevention and control office

List of Tables:

List of Figures

Abstract

Background: Visceral Leishmaniasis (VL) is a vector-born disease that is caused by an obligate intra-cellular protozoan parasite. Among parasitic diseases Leishmaniasis is the second deadly parasitic disease next to malaria. Ethiopia is one of the six countries in which more than 90% of global VL cases occur. Knowing the recent prevalence and associated factors for Visceral Leishmaniasis-HIV co infection will help in the control of the disease.

Objective: To assess Visceral Leishmaniasis - human immunodeficiency virus (HIV) co infection and associated factors among adult Visceral Leishmaniasis patients admitted at University of Gondar hospital, Gondar town, North West Ethiopia.

Methodology: A cross sectional retrospective review study was conducted on all (465) patients with Visceral Leishmaniasis who had been admitted at University of Gondar hospital from September 11, 2011 to June 30, 2013. Descriptive statistics like Frequency tables, charts, mean with standard deviation and percentages were used to present and summarize most of the variables. Both bivariate and multivariate logistic regression analysis were used to identify factors associated with Visceral Leishmaniasis - HIV co infection.

Result: Out of the total study subjects 55 (11.8%) were Visceral Leishmaniasis -HIV co-infected patients. Age 28-37 years [AOR= 9.56; 95% CI: 4.10-22.31], >37 years [AOR= 4.16; 95% CI: 1.32-13.06]) and type of residence (AOR=4.88, 95% CI 2.59-9.20) were found to be significantly associated with VL-HIV co infection.

Conclusion and recommendation: Visceral Leishmaniasis-HIV co infection prevalence was found to be lower than the other studies. Age and type of residence were variables found to be significantly associated with Visceral Leishmaniasis-HIV co infection. Ministry of health and other None Governmental organizations (NGOs) should implement intervention strategies to reduce further the Visceral Leishmaniasis-HIV co infection rate as a whole and particularly among the resident population of VL endemic area.

1. Introduction

Visceral Leishmaniasis (VL), also called kala-azar, is a vector-born disease that is caused by obligate intra-cellular protozoan parasites. They are members of the Leish mania donovani complex (*L*. *donovani* and *L. infant*) and transmitted by female phlebotomine sand flies (Old World) and Lutzomyia (New World). VL is endemic in semi arid and arid areas and mainly affects the world's poorest populations (1).

Among parasitic diseases Leishmaniasis is the second deadly disease next to malaria (2); and VL is the most severe form of Leishmaniasis that is almost always fatal if left untreated. Over 90% of the estimated annual cases of 500,000 VL worldwide occur in just six countries: Bangladesh, India, Nepal, Sudan, Ethiopia and Brazil. When we come to our continent, Eastern Africa has the second highest number of VL cases, after the Indian Subcontinent (3, 4).

Historically the first case of VL in Ethiopia was identified in 1942 in southern Ethiopia. According to one study, annually an estimated 3700–7400 cases occur in Ethiopia (5). VL now poses a significant public health problem in Ethiopia with expanding endemic areas. When we see the Local Geographical distribution, VL is found in Tigray, Amhara, Oromia, Afar, Somali and SNNPR (6). In the north, the responsible vector (the female phlebotomine sand fly) is associated with Acacia-Balanites forest, and in the south with termite hills (5, 7).

The north-western VL focus in Ethiopia covers the semi-arid Metema and Humera plains in Amhara and Tigray regional states respectively. Historically, this area reported only sporadic cases, but a marked increase occurred during the 1970s when migrants from the non-endemic highlands began to arrive in the area to harvest crops on the large-scale agricultural introduced at the time (8-13).

The development of HIV/AIDS pandemic during the last 25 years has modified the spectrum of Leishmaniasis in clinical, diagnostic and epidemiological implication. From

middle of 1980s, when the first case of Leishmaniasis associated with HIV was notifeid, an increase in the case of co infection has been registered; to date cases in 35 countries have been detected (14). In East Africa more worryingly, particularly Sudan and North West Ethiopia are facing a surge in Leishmaniasis/ HIV co-infection, evidenced With reporting co-infection rate 34% (15).

HIV co-infection has become a major complication of Leishmaniasis and ignited calls for the recognition of Leishmaniasis as AIDS defining illness. For both VL and HIV attack the immune system of the body, they produce profound immune deficiency state. The result and effect of this state is that VL accelerates the onset of full-blown AIDS and shortens the life expectance of HIV-infected people (16, 17)

VL-HIV co-infection is characterized by a number of complexities including challenging diagnosis and treatment. The standard serological tests are often less reliable in HIV co-infection, atypical VL presentation is common. In terms of treatment, VL-HIV co-infection is characterized by high mortality, increased drug toxicity and overall poor treatment response. Moreover, even with initiation of antiretroviral treatment, multiple VL relapses remain common. VL relapses tend to be associated with gradual loss in treatment responsiveness. There are also concerns that VL-HIV co-infected individuals could serve as a source and reservoir of drug resistant parasites

Although there have been studies showing VL-HIV co infection prevalence rate in North West Ethiopia still it is very important to study the prevalence at this point in time. Knowing the progress of VL-HIV co infection rate is very crucial in the control of VL as it is becoming an emerging disease in the area. (18)

2. Literature review

Several studies showed the incubation period of VL typically is to be 2-6 months but may be shorter or much longer (19). Once the parasite gets an access in to the host's body then it migrates to the internal organs such as liver, spleen (that is why called visceral) and bone marrow. VL If left untreated will almost always result in death of the host. According to WHO, the clinical presentations of VL include prolonged high grade fever (2 weeks or more), with remittent, intermittent or continuous characteristics, splenomegaly, weight loss, anemia, cough, epistaxis, hepatomegaly and body weakness. In rare occasions some patients will present with edema, jaundice, vomiting, joint pain, abdominal pain, lymphadenopathy and diarrhea (20).

Even though the clinical presentation of VL is largely similar in the various endemic areas there are also some differences between individuals and according to geographic foci (21). For example lymph nodes are rarely found in Indian VL patients but are frequent in Sudanese VL patients. The other example is hyper pigmentation which lead to the name Kala-azar (black fever in Hindi), has been more described in VL patients from the Indian subcontinent. (22).

Clinical features of cases of VL in HIV infected patients do not differ significantly from those in immune competent patient. However the clinical presentation of VL in HIV infected individuals can be atypical in severely immunocompromized patients (23).

In one study that patients with a CD4 count of <50 cells/mm2 had a lower frequency of the clinical triad of fever, spleenomegally and hepatomegally. In the same study, diarrhea or epigastragia was symptomatic in severely immunocopromized HIV infected individuals as the result of the atypical location of the leishmania parasitization of the digestive tract (24).From atypical features of VL, leishmanial involvement of the skin was seen (8.2%)in HIV infected patients, but none of the HIV negative patients . As to a result of one comparative study done in Spain, concerning diagnostic procedures of a constant finding in HIV infected individuals with VL has low sensitivity (50% versus 80%; of the serologic test of VL-HIV co infected and non HIVcoinfected VL patients respectively (25).

The spread of human immunodeficiency virus (HIV) infection to areas where visceral Leishmaniasis (VL) is endemic has become a major challenge to the control of VL infection (26). A good example is that, in 1995 the first reported seven cases of HIV and Leishmania co infection in Ethiopia was found increased to 72 by 1998 (25). The other example in Southern Europe, up to 70 per cent of VL cases with HIV infection had been reported (27).

The epidemiological characteristics of VL- HIV co-infection can differ from one endemic region to another due to parasite strain, vector behavior or socio-environmental conditions of the exposed hosts in the VL-HIV co infection, factors that were associated differently from population to population due to different reasons. According to the study in Europe, it was known that people sharing needles were the main risk group to the anthroponetic transmission of both infections. (28).

When we see one local study result, in humera, Tigray, the risk factors of VL-HIV co infection considered were population mobility and socioeconomic problems. According to the result of the study, 23% migrants and 40% of residents were HIV positive (29).

Conceptual Framework

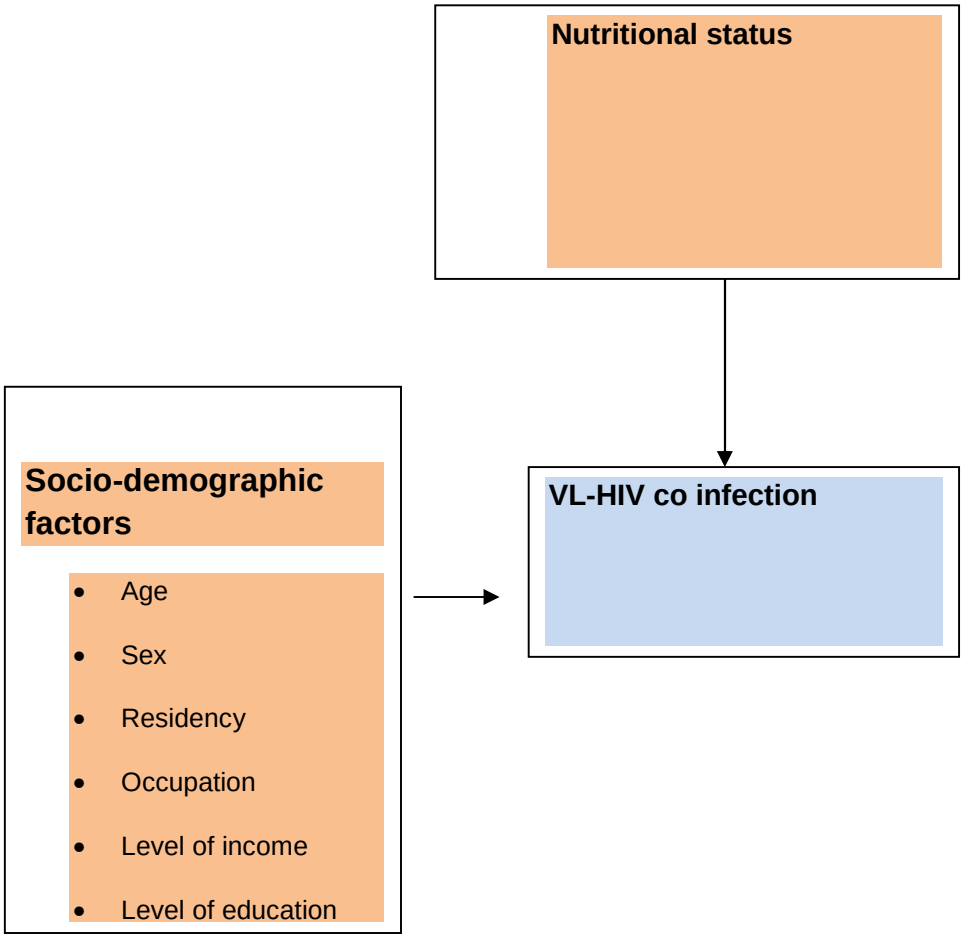

Figure 1: Conceptual frame of VL-HIV co infection and associated factors

3. Significance of the study

VL is one of the neglected diseases that is spreading to previously non-endemic areas. This study will assess the prevalence of VL-HIV co infection and the factors that contribute to the spread of the disease. Knowing the recent prevalence and contributing factors for VL-HIV co infection will help in the control of the disease. Hopefully the study result will help the concerned bodies to intervene or to address the problem accordingly and will be serving as a source of information to different type of stake holders and partner's serving to make possible interventions.

4. Objectives of the study:

4.1. General objective:

To assess VL-HIV co infection and associated factors among VL patients admitted at University of Gondar Hospital.

4.2 Specific objective

1. To determine the prevalence of VL-HIV co infection among VL patients in university of Gondar Hospital.
2. To identify factors associated with VL- HIV co-infection among VL patients in university of Gondar Hospital.

5. Methodology:

5.1. Study design

A cross sectional retrospective review of clinical records was used to conduct

5.2. Study area and period:

The study area was UoGH. The hospital is a teaching and referral hospital located 738 Kms North West of Addis Ababa. UoGH is in close proximity to the main VL endemic area in the country. It has a Leishmaniasis research and treatment center that gives diagnosis and treatment service to Leishmaniasis patients. This center was established in 2005 and has 24 inpatient beds. The study was conducted from June 1st to July 31st, 2013.

5.3 Source population:

All VL patients who had been admitted from September 11, 2011 to June 30, 2013 in the hospital were used.

5.4 Study subjects:

Adult VL patients (≥ 18 years old) who were diagnosed for VL by using parasitological methods and serological positive result test from 2011-2013 were included.

5.5 Inclusion and exclusion criteria:

Inclusion criteria:

- VL patients diagnosed with demonstration of LD bodies from aspirates.
- VL patients diagnosed by clinical plus positive serological test.

Exclusion criteria:

- Patient charts with incomplete information of variables.
- Patients with unknown status of HIV.
- Patients with malaria co infection confirmed

5.6 Sample size:

All VL patients who were admitted at Gondar university hospital meeting the inclusion criteria were included.

5.7 Sampling procedure:

All VL patients who had been admitted at Gondar University Hospital meeting the inclusion criteria were included.

5.8 Study variables:

Dependent variables:

VL-HIV co infection

Independent variables:

Age, Sex,

Place of residence, Nutritional status

5.9 Data collection tools and procedures:

Data was collected by a health professional working in the Leishmaniasis research and treatment center from patient chart. Patient's charts were reviewed to collect data from documented patients' history, physical examinations and laboratory findings.

5.10 Data quality assurance procedures:

Data was collected by an experienced health professional working at the Leishmaniasis research and treatment center of UoGH. The data collectors were properly informed how to collect the data from the patients charts.

5.11 Data management and analysis:

Data was coded and entered using SPSS for windows version 16. Missing values and data clearance were checked. Frequency tables, percentages were used. Bivariate analysis was conducted primarily to check which variables had association with the dependent variable individually. Variables found to have association with the dependent variables were then entered in to multivariate logistic regression for controlling the possible effect of confounders and finally the variable which had significant association were identified on the basis of OR, with 95%CI and 0.05 p-values.

5.12 Ethical considerations:

Ethical clearance was obtained from Institutional review board of University of Gondar, Prior to enrolment supporting letter was obtained from UGH clinical director's office. All the data obtained from the patients chart was kept confidential at all times.

6. Result:

6.1 Socio-demographic characteristics

Almost all of the study subjects (99.8 %) were males. The mean age was 25.19 ± 6.43 years. A higher number of VL patients were in the age group between 18-27 years, 72.3%. Majority of VL patients were temporary residents (migrants) to endemic areas 79.4 (Table 1).

Table 1. Socio demographic characteristics of VL patients (n=465), UoGH, Northwest Ethiopia, 2013

Variables		frequency	Percentage (%)
Sex			
	Male	464	99.8
	Female	1	0.2
Age			
	18-27	336	72.3
	28-37	98	21.1
	>=38	31	6.7
Residency			
Permanent	Resident	96	20.6
Migrant (Temporary	resident)	369	79.4

6.2 Clinical manifestations and laboratory findings of VL patients

Fever was found to be the most commonly reported symptom (97%) followed by weight loss (94.2%), loss of appetite (92.9%), body weakness (72%), and cough (58.6%). Majority of the patients, (93.5%) have history of travel to VL endemic areas and patients with fever more than 2 weeks were to account (96.3%) and less than 2 weeks 3 (0.6%) (Table 2).

The most frequent objective findings were spleenomegally (96.3%), pal mar pallor (75.3%) and pedal edema (32.3%).Concerning the nutritional status of VL patients, (87.9%) had malnutrition. From these, mild to moderate malnutrition was found in (48.1%) and (39.8%) were severely malnourished. As to the laboratory result, we see leucopenia (98.5%), anemia (92.5%), and thrombocytopenia (91.2%), elevated SGOT (82.4%), elevated SGPT (42.2%), increased creatinine (15.3%) and increased BUN (11%) (Table 2).

Table 2. Common clinical manifestations and laboratory findings of VL patients, UoGH, Northwest Ethiopia, 2013

		No. and % of patients with VL		All N= 465 (%)
		HIV positive (n=55)	HIV negative (n= 410)	
Fever	Yes	42	409	451 (97)
	No	13	1	14 (3)
Duration of fever	>2weekss	42	406	448 (96)
	<2weeks	0	3	3 (0.6)
Weight loss	yes	53	385	438(94.2)
	no	2	25	27 (5.8)
Loss of appetite	yes	52	380	432 (92.2)
	no	3	30	33 (7.1)
Body weakness	yes	43	292	335 (72)
	no	12	118	130 (28)
Cough	yes	30	238	268 (57.6)
	no	25	172	197 (42.2)
Epitasis	yes	14	154	168 (36.1)
	no	41	256	279 (63.9)
Dragging sensation	yes	11	81	92 (19.8)
	no	44	329	373 (80.2)
Diarrhea	yes	19	46	65(14)
	no	36	364	400(86)
Nausea and vomiting	yes	6	47	53 (11.4)
	no	49	363	412 (88.6)
Palmer pallor(pale conjunctiva)	yes	35	315	350 (75.3)
	no	20	95	115(24.7)
Pedal edema	yes	13	139	150 (32.3)
	no	44	271	315 (67.7)

Jaundice	yes no	8 47	59 351	67 (14.4) 398 (85.6)
Spleenomegally	yes no	51 4	397 13	448 (96.3) 17 (3.7)
Hepatomegally	yes no	14 41	57 353	71 (15.3) 394 (84.7)
Lymphadenopathy	yes no	3 52	21 389	24 (5.2) 441 (94.8)
Skin color change	yes no	1 54	3 470	4 (0.9) 461 (99.1)
BMI	Severe malnutrition <16kg/m2	19	166	185 (39.8)
	Mild to moderate malnutrition 16-18.49 kg/m2	30	194	224 (48.2)
	Normal (≥18.5 kg/m2)	6	50	56 (12)
Leucopenia	yes no	53 2	405 5	458 (98.5) 7 (1.5)
Anemia	yes no	52 3	378 32	430 (92.5) 35 (7.5)
Thrombocytopenia	yes no	43 12	381 29	424 (91.2) 41 (8.8)

Elevated SGOT	Elevated	44	225	269 (57.9)
	Not elevated	11	185	196 (42.1)
Elevated SGPT	Elevated	19	63	82 (17.6)
	Not elevated	36	347	383 (82.4)
BUN	Increased	6	45	51(11)
	Normal	49	365	414 (89)
Creatinine	Increased	9	62	71(15.3)
	Normal	46	348	394 (84.7)

7.3 Laboratory diagnosis for VL

The most commonly used method of VL diagnosis was parasitological (92.9%) and the other method used was serologic test (7.1%). Parasitological confirmation was carried out for (92%) HIV negative and (100%) HIV positive patients. Sites

that were used for aspiration were spleen, bone marrow and lymph node that each account for (62.6%), (29.2%) and (1.1%) respectively. Spleenic aspiration was the commonest procedure employed in (61.7%) HIV negative and (69.1%) in HIV positive patients followed by bone marrow puncture (29.3%) for HIV negative and (29.1%) HIV positive patients. Lymph node aspiration was done in (1%) HIV negative and (1.8%) HIV positive patients.

7.4 Prevalence of VL- HIV co infection

Among the total 465 study subjects the prevalence of VL-HIV co infection was found to be 11.8% (figure 3).

Looking at different age categories, prevalence of VL-HIV co infection patients in the age category between 18-27 years had 5.7%, 28-37 years had 26.5% and >37 had 32.3%. The prevalence of VL-HIV co infection among residents and migrants was found to be 29.2% and 7.3% respectively (Table 2).

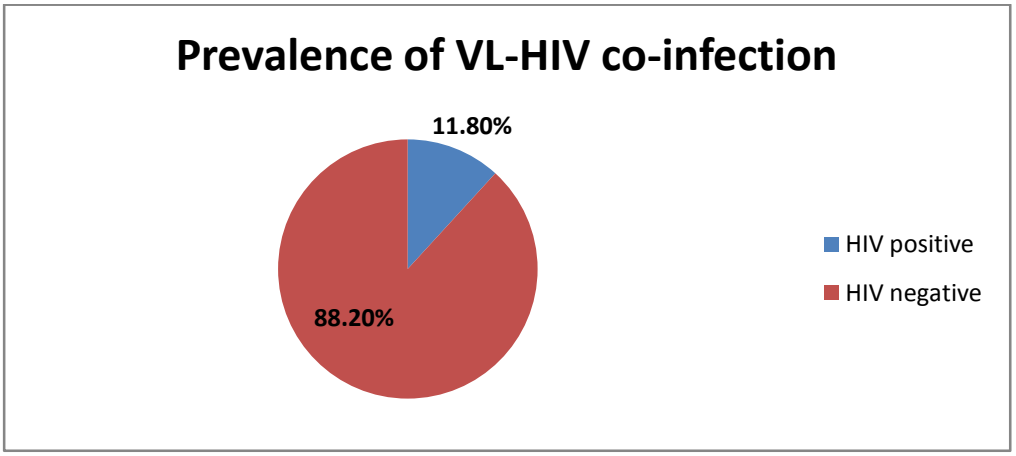

Figure 2: Prevalence of VL- HIV co infection, UoGH, Northwest Ethiopia, 2014

7.5 Factors associated with VL-HIV co-infection

The association between selected socio-demographic variables on VL-HIV confection of the Study participants was investigated using both bivariate and multivariate logistic regression techniques. Variables with significant association considered in the bivariate and multivariate logistic regression analysis were age and residence. Accordingly, VL patients in the age group between 28-37 years were 6 times more likely to have VL-HIV co infection[AOR= 6.16; 95% CI: 3.14-12.01]and the age group >37 years were found to be about 6 times more likely to be VL-HIV co infected [AOR= 5.98; 95% CI: 2.35-5.25]. Permanent residents were about 5 times more likely to acquire VL-HIV co infection when compared to temporary residents (migrants) [AOR=4.88, 95% CI 2.59-9.20] (Table 3).

Table 3. Factors in VL-HIV co infection, UoGH, Northwest Ethiopia, 2013

	HIV status				
	HIV positive (n=55)	**HIV negative (n=410)**	**All N= 465 (%)**	**COR (95% CI)**	**AOR (95% CI)**
Age					
18-27	19 (34.6)	317 (77.3)	336(72.3)	1	
28-37	26 (47.3)	72 (17.6)	98(21.1)	6.02(3.16-11.48)**	6.16 (3.14-12.07)**
>37	10 (18.2)	21 (5.1)	31(6.7)	7.94(3.28-19.23)*	5.98 (2.35-5.25)**
Residency					
Resident	28 (50.9)	68 (16.6)	96(20.6)	5.21(2.89-9.40)**	4.88 (2.59-9.20)**
Migrant	27(49.1)	342 (83.4)	369(79.4)	1	

7. Discussion:

In this study almost all VL patients (99.8%) were males and the result is similar to previous report (96.3%) in the same study area (23). A higher proportion of VL patients were temporary residents (migrants) 79.4 % and the possible reason for this could be a higher number of non immune (previously unexposed) daily laborers population migrations to the endemic areas (29).

VL patients in the age group between 28-37 years and >37 years were found more likely to be VL-HIV co infected when compared to the age group between 18-27 years. A similar result was reported by a study conducted in the same area that had reported mean age of HIV-positive patients was significantly higher than for HIV-negative patients 32.2(7) vs 23.5(5.7), OR= 0.78, 95% CI 0.75–0.85, P < 0.001) (30).

In this study significant association was found with residence and VL- HIV co-infection. A higher proportion of HIV positives 28 (50.9%) were residents compared to 68 (16.6%) HIV negative patients (AOR= 4.88, 95% CI 2.59-9.20). This could be due to the fact that HIV infected residents have lifelong exposure time and risk to be infected and develop the disease than migrants. This is supported by a result from a study which showed a higher risk for migrants who had spent a year or more in an endemic area compared to those with shorter duration of exposure. A report in 2008, KAH (Humara, North west Ethiopia) treated a total of 376 VL patients of whom 23% of migrants and 40% of residents were HIV positive (MSF-H, unpublished data) (28). ‘

According to the finding of this study the prevalence of VL-HIV co infection is 11.8%. This is lower than a study conducted in the same study area that reported 38.2% VL-HIV co infection prevalence (30). This difference could be explained by decreasing prevalence of HIV in the country in general. The HIV/AIDS Prevention and Control Office (FHAPCO) reported that adult HIV prevalence level has fallen from 2.1% in 2011 to 1.3% in 2013. According to FHAPCO report, expanded HAART service in the health care facilities could have improved immune status of HIV patients that helps the individuals not to develop the disease. The HAART service expansion also explained that in 2001 there were only three ART centers but the number has increased to 838 in 2013 (31).The effect of HAART other than Ethiopia showed that the number of co

infected individuals in European countries where the disease is endemic, fell sharply (32, 33 and 34).Another study result showed when Comparing to those who received no antiretroviral therapy, Patients treated with highly active antiretroviral therapy (HAART) had a 59% reduction of risk for developing the disease (32).

8. Limitation of the study:

This study was conducted on secondary data because of this important information of some variables were not found.

9. Conclusion:

The overall HIV-VL co-infection rate was found to be lower when compared to previous studies done in the same study area. Age and residency were found to be significantly associated factors that contribute for VL-HIV co-infection. Age group between 28-37 years and >38 years were found to be at higher risk for VL-HIV co infection. A higher VL-HIV co infection prevalence rate was found among endemic area permanent residents than temporary residents (migrants).

10. Recommendation

Ministry of health should implement intervention strategies to avert the high VL-HIV co infection rate among endemic area residents. These can include early identification of HIV cases and giving health education about VL-HIV co infection to create awareness. In addition expansion of HAART service in the health care system of endemic areas is important. Otherwise further research needs to be carried out to identify the reason why VL-HIV co infection rate is high among endemic residents than migrants.

Ministry of health should also give attention to the age 28 years and above to reduce their risk for VL-HIV co infection.

References:

1. Mueller YK, et al. Burden of Visceral Leishmaniasis in Villages of Eastern Gedaref State, Sudan: An Exhaustive Cross-Sectional Survey. *PLoS Negl Trop Dis*. 2012; 6(11): 1872.
2. Desjeux P. "The increase of risk factors for Leishmaniasis worldwide". *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2001; 95 (3): 239–43.
3. Desjeux P, et al. Leishmaniasis: current situation and new perspectives. *Comp Immunol Microbiol Infect Dis*. 2004; 27: 305-18.
4. Chappuis F, et al. Visceral Leishmaniasis: what are the needs for diagnosis, treatment and control? *Nat Rev Microbiol*. 2007; 5: 873-82.
5. Aseffa A. Armauer Hansen Research Institute/ALERT- Consultative Meeting on the Control of Leishmaniasis in the African Region. Addis Ababa: WHO/AFRO, 2010.
6. Deribe et al. The burden of neglected tropical diseases in Ethiopia, and opportunities for integrated control and elimination. *BioMed Central Parasites & Vectors*. 2012; 5:240.
7. Alvar J, et al. Leishmaniasis Worldwide and Global Estimates of its incidence. *PLoS One*. 2012; 7(5):35671.
8. Tekle A. et al. Kala-azar in Humera (Northwest Ethiopia). *Parassitologia.* 1970; 12: 21-25.
9. Ashford R. et al. The epidemiology of cutaneous Leishmaniasis in Ethiopia. *Trans R Soc Trop Med Hyg*, 1973; 67: 568-601.
10. Fuller G. et al. Kala-azar in Ethiopia I: Leishmanin skin test in Setit Humera, a kala-azar endemic area in northwestern Ethiopia. *Ann Trop Med Parasitol*. 1976b; 70: 147-63.
11. Mengesha B. & Abuhoy M. Kala-azar among labour migrants in Metema-Humera region of Ethiopia. *Trop Geogr Med*. 1978; 30: 199-206.
12. Maru M. Clinical and laboratory features and treatment of visceral Leishmaniasis in hospitalized patients in Northwestern Ethiopia. *Am J Trop Med Hyg*. 1979; 28: 15-8.

13. Hailu, A. & Frommel D. The Ecology of Health and Disease in Ethiopia. Leishmaniasis in Ethiopia Boulder, Colorado, USA: West view Press; 1993.
14. Cruz.et al. Leis mania/HIV co-infections in the second decade. Indian J Med Res. 2006; 123: 357-388.
15. Talha Burki. East African countries struggle with visceral Leishmaniasis. *The Lancet*. 2009; 374(9687): 371 – 372.
16. R.K. Singh, H.P. Pandey & S. Sundar. Visceral Leishmaniasis (kala-azar): Challenges ahead. *Indian J Med Res*. 2006; 123: 331-344.
17. WHO: Report of the Fifth Consultative Meeting on Leis mania /HIV Co infection Addis Ababa, Ethiopia, World health organization; 2007.
18. Rachel ter Horst1, et al. Concordant HIV Infection and Visceral Leishmaniasis in Ethiopia: The Influence of Antiretroviral Treatment and Other Factors on Outcome. Clin Infect Dis.2008; 46 (11): 1702-1709.
19. François Chappuis, Shyam Sundar, Asrat Hailu, et al. Visceral Leishmaniasis: what are the needs for diagnosis, treatment and control?. *Nature Publishing Group*.2007; 5: 873-876.
20. Dr. S. K. Sharif, et al. Diagnosis and Management of Visceral Leishmaniasis (Kala Azar) National Guidelines for Health Workers. Kenya: *Republic of Kenya ministry of public health and sanitation*. 2012; 6.
21. Muhammad Uzair, et al. Visceral Leishmaniasis (kala-azar): presentation, diagnosis and response to therapy (an experience of ten cases in adults), *Gomal Journal of Medical Sciences*. 2004; 2(1): 9-11.
22. François Chappuis, Shyam Sundar, Asrat Hailu, et al. Visceral Leishmaniasis: what are the needs for diagnosis, treatment and control?. *Nature Publishing Group*.2007; 5: 873-876
23. Alvar J, Canavate C, Gutierrez-Solar B, et al. *Leis mania* and human immunodeficiency virus co infection: the first 10 years. Clin Microbiol Rev **1997**; 10: 298–319.
24. Rosenthal E, Marty P, del Giudice P, et al. HIV and Leis mania co infection: a review of 91 cases with focus on atypical locations of Leis mania. Clin Infect Dis 2000; 31:1093.

25. Pint ado Vicente, et al. Visceral Leishmaniasis in Human Immunodeficiency Virus (HIV)-Infected and Non-HIV-Infected Patients: A Comparative Study. *Medicine*. 2001; 80(1): 54-73.
26. Hailu A, Berhe N. The performance of Direct Agglutination Test (DAT) in the diagnosis of visceral Leishmaniasis among Ethiopian patients with HIV co-infection. Ann Trop Med Parasitol 2002; 96: 25-30.
27. Berhe N, Hailu A, Walday D, Negesse Y, Cenini P, Frommel D. Ethiopian visceral Leishmaniasis patients co-infected with human immuno deficiency virus. Trans RSoc Trop Med Hyg 1995; 89 : 205-7.
28. Desjeux P UNAIDS. Leis mania and HIV in Gridlok-Document WHO/CTD/LEISH/98.9 Add. 1, UNAIDS/98.23.Geneva: World Health Organization; 1998.
29. Priscilla Alexandrino-de-Oliveira**,** Joanna Reis Santos-Oliveira**,** Maria Elizabeth Cavalheiros Dorval,et al. HIV/AIDS-associated visceral Leishmaniasis in patients from an endemic area in central-west Brazil. Mem Inst Oswaldo Cruz. 2010; 105(5): 692-697.
30. Daniel Argaw, Abate Mulugeta, Merce‘ Herrero, et al. Risk Factors for Visceral Leishmaniasis among Residents and Migrants in Kafta-Humera, Ethiopia. PLOS Neglected Tropical Diseases. 2013; 7(11): e2543.
31. Mengesha B, and Abuhoy M., Kala-azar among Labor migrants in Metema-Humera region of Ethiopia. Trop geogr Med 1978; 30:199-206.
32. Zewdu Hurissa, et al. Clinical characteristics and treatment outcome of patients with visceral Leishmaniasis and HIV co-infection in northwest Ethiopia. Tropical Medicine and International Health. 2010; 15 (7), 848–855.
33. FHAPCO, Report on HIV/AIDS Prevalence rate in Ethiopia, 2013.
34. Del Giudice, P., et al. Impact of highly active antiretroviral therapy on the incidence of visceral Leishmaniasis in a French cohort of patients infected with human immunodeficiency virus. J. Infect. Dis. 2002; 186**:**1366-1370.
35. . Velez, R. The impact of highly active antiretroviral therapy (HAART) on visceral Leishmaniasis in Spanish patients who are co-infected with HIV. Ann. Trop. Med. Parasitol. 2003; 97(Suppl. 1)**:**143-147.

36. Russo, R., L. Nigro, G. Panarello, and A. Montineri. Clinical survey of Leis mania/HIV co-infection in Catania, Italy: the impact of highly active antiretroviral therapy (HAART). Ann. Trop. Med. Parasitol. 2003; 97(Suppl. 1)**:**149-155.

Annex i: Data collection instrument

Demographic characteristics:

1. Age in years: _____
2. . Sex: 1. Male 2. Female

3. Place of residence: To which of the following categories the subject belongs to the kalazar endemic areas?

1. Permanent 2. Migrant

I. Subjective findings:

1. History of fever? 1. Yes 2. No
2. History of fever for how long? 1. < 2 wks 2. > 2 wks
3. Rigors and chills associated with fever? 1. Yes 2. No
4. History of sweating? 1. Yes 2. No
5. History of body weakness? 1. Yes 2. No
6. History of chills and rigors? 1. Yes 2. No
7. History of vertigo? 1. Yes 2. No
8. History of Tinnitus? 1. Yes 2. No
9. History of blurring of vision? 1. Yes 2. No
10. History of headache? 1. Yes 2. No
11. History of loss of appetite? 1. Yes 2. No
12. History of weight loss? 1. Yes 2. No
13. History of body weakness? 1. Yes 2. No
14. History of nausea and vomiting? 1. Yes 2. No
15. History of diarrhea? 1. Yes 2. No
16. History of cough? 1. Yes 2. No

17. History of epitasis? 1. Yes 2. No
18. History of travel to kala-azar endemic area? 1. Yes 2. No
19. History of drugging sensation on the LUQ area? 1. Yes 2. No

II. Objective findings:

1. Weight (KG):_____ Height (cm):_____BMI:_____
2. Body temperature (In Celsius):_____
3. Palpable spleen 1. Yes 2. No
4. Hepatomegally 1. Yes 2. No
5. Jaundice of the sclera 1. Yes 2. No
6. Pain less palpable lymph nodes 1. Yes 2. No
7. Palmar pallor/ pale conjunctiva 1. Yes 2. No
8. Pethichial rush 1. Yes 2. No
9. Skin change- gray/dark 1. Yes 2. No
10. Pedal edema 1. Yes 2. No
11. Site of aspiration? 1. Spleenic 2. Bone marrow 3. Lymph node
12. Diagnosis? 1. Parasitic 2. Serologic
13. Other objective findings:

_____

III. Laboratory findings:

1. Serological test (rK39) 1. Pos 2. Neg
2. LD body isolation: 1. Yes 2. No
3. Hemoglobin (gm/dl):_____
4. Platelet count: _____
5. Total WBC: _____
6. Neutrophils: _____
7. Lymphocytes: _____
8. Liver enzyme: SGOT_____ SGPT_____
9. Renal function test BUN_____ Creatinine_____

10. HIV status: 1. Negative 2. Positive 3. Missing/not done

11. Cd4 count: _____

Thesis submission form

Declaration

I, the undersigned, MSC student of Clinical tropical infectious diseases and HIV medicine declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Master of Public Health.

Name: Girma Worede

Signature: _____

Place of submission: Department of internal medicine, College of Medicine and Health Sciences, University of Gondar.

Date of Submission: _____

This thesis work has been submitted for examination with the approval of my advisors.

Advisors:

Name	Signature
1. Dr. ERMIAS DIRO	_____
2. Ato TERESA KISI	_____